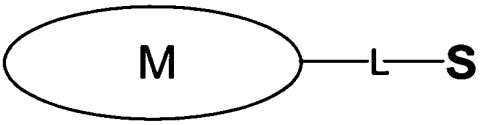
CLAIMS

1. A compound of the formula:



I

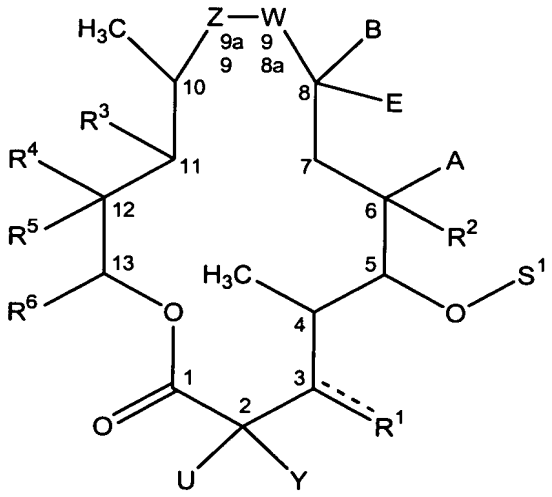
wherein

(i) **M** is a macrolide subunit selected from the group consisting of multi-member lactonic ring molecules, wherein "member" refers to the number of carbon atoms or heteroatoms in the lactonic ring and "multi" signifies a whole number greater than about 10, and up to about 18 said molecules having the property of accumulating within mammalian, including human, immune system cells that mediate inflammatory immune responses;

(ii) **S** is a steroidal anti-inflammatory subunit; and

(iii) **L** is a linker molecule to which each of **M** and **S** are covalently linked.

2. The compound according to claim 1 wherein **M** represents a group of Formula **II**:



II

wherein

(i) Z and W independently are >C=O, $>CH_2$, $>CH\text{-}NR_tR_s$, $>N\text{-}R_N$ or $>C=N\text{-}R_M$, wherein

R_t and R_s independently are hydrogen or alkyl;

R_M is hydroxy, alkoxy, substituted alkoxy or OR^p;

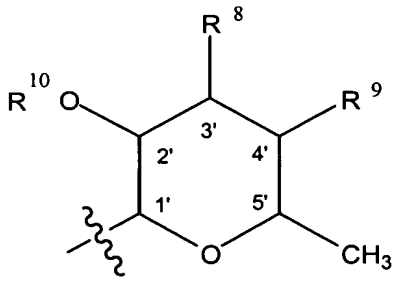
R_N is hydrogen, R^p , alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or $-C(X)\text{-}NR_tR_s$; wherein X is =O or =S;

provided that Z and W cannot both simultaneously be, >C=O, $>CH_2$, $>CH\text{-}NR_tR_s$, $>N\text{-}R_N$, $>C=N\text{-}R_M$ or a bond;

(ii) U and Y independently are hydrogen, halogen, alkyl, or hydroxyalkyl;

(iii) R^1 is hydroxy, OR^p , $-O\text{-}S^2$ group or an =O;

(iv) S^1 is a sugar moiety of Formula **III**:



III

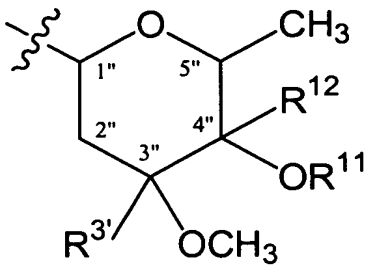
wherein

R^8 and R^9 are both hydrogen or together form a bond, or R^9 is hydrogen and R^8 is $-N(CH_3)R^y$, wherein

R^y is R^p, R^z or $-C(O)R^z$, wherein R^z is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with C_2-C_7-alkyl, C_2-C_7-alkenyl, C_2-C_7-alkynyl, aryl or heteroaryl;

R^{10} is hydrogen or R^p;

(v) S^2 sugar moiety of Formula **IV**:



IV

wherein

$R^{3'}$ is hydrogen or methyl;

R^{11} is hydrogen, R^p, or O-R^{11} is a group that with R^{12} and with C/4" carbon atom forms a >C=O or epoxy group;

R^{12} is hydrogen or a group that with O-R^{11} group and with C/4" carbon atom forms a >C=O or epoxy group;

(vi) R^2 is hydrogen, hydroxy, OR^p or alkoxy ;

(vii) A is hydrogen or methyl;

(viii) B is methyl or epoxy;

(ix) E is hydrogen or halogen;

(x) R^3 is hydroxy, OR^p , alkoxy or R^3 is a group that with R^5 and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate, or if W or Z is >N-R_N R^3 is a group that with W or Z forms a cyclic carbamate;

(xi) R^4 is C_1-C_4 alkyl;

(xii) R^5 is hydrogen, hydroxy, OR^p , C_1-C_4 alkoxy, or a group that with R^3 and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate;

(xiii) R^6 is hydrogen or C_1-C_4-alkyl;

wherein **M** has a linkage site through which it is linked to **S** *via* linking group **L**; provided that the linkage site being at one or more of the following:

a) any reactive hydroxy, nitrogen, or epoxy group located on S^1, S^2, or an aglycone oxygen if S^1 and/or S^2 is cleaved off;

b) a reactive >N-R_N or -NR_tR_s or oxo group located on Z or W;

c) a reactive hydroxy group located at any one of R^1, R^2, R^3, and R^5;

d) any other group that can be first derivatized to a hydroxy or -NR_tR_s group and

R^p is hydroxyl or amino protective group.

3. The compound according to claim 1 wherein **L** represents a group of Formula **VA** or of Formula **VB**:

VA X^1-$(CH_2)_m$-X^2

VB X^1-$(CH_2)_m$-Q-$(CH_2)_n$-X^2

wherein

X^1 is selected from: -CH_2-, -CH_2NH-, -C(O)-, -OC(O)-, =N-O- or -OC(O)NH-; -C(O)NH;

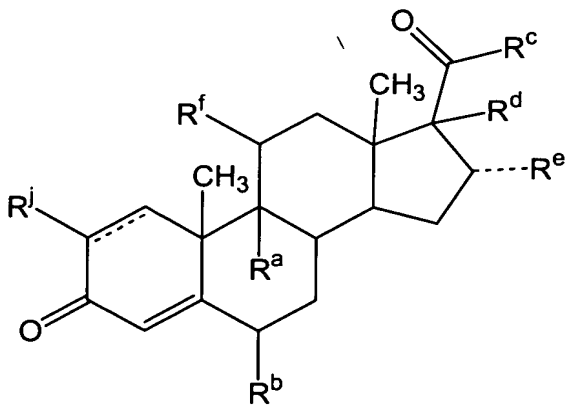
X^2 is -NH- or -NHC(O)- or -CH_2-;

Q is -NH- or -CH_2-, wherein

each -CH_2- or –NH- group may be optionally substituted by C_1-C_7-alkyl, C_2-C_7-alkenyl, C_2-C_7-alkynyl, C(O)R^x, C(O)OR^x, C(O)NHR^x, wherein R^x may be C_1-C_7-alkyl, aryl or heteroaryl;

the symbols m and n independently are a whole number from 0 to 8, with the proviso that if Q is NH, n cannot be 0.

4. The compound according to claim 1 wherein **S** represents a group of Formula **X**:



X

wherein

R^a and R^b independently represents, hydrogen or halogen;

R^c is hydroxy, alkoxy, alkyl, thiocarbamoyl, carbamoyl or a valence-bond;

R^d and R^e independently represents: hydrogen, hydroxy, methyl or C_1-C_4-alkoxy or each are a group that forms a 1,3-dioxolane ring with the other or a valence bond;

R^f is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;

R^j is hydrogen or halogen.

5. The compound according to claim 2 wherein

Z is $>NR_N$, wherein R_N is hydrogen or a methyl group;

W is $>CH_2$;

B is methyl;

E is hydrogen;

R^2 is hydroxy;

A is methyl;

S^1 group represents a group of Formula **III** wherein

R^8 is selected from: hydrogen, amino, *N*-metylamino, *N*,*N*-dimethylamino, *N*-methyl-*N*-(C_2-C_4)-alkylamino, *N*-methyl-*N*-methylcarbonylamino, *N*-methyl-*N*-benzylamino, *N*-methyl-*N*-cyclohexylamino;

R^9 and R^{10} are hydrogen;

R^1 is O-S^2 wherein S^2 represents a group of Formula **IV** wherein R^{11} and R^{12} are hydrogen and R^{13} is methyl;

U is hydrogen;

Y is methyl;

R^4 is methyl;

R^6 is ethyl;

R^5 is hydroxy or a group that with R^3 and with C/11 and C/12 carbon atoms forms a cyclic carbonate bridge;

R^3 is hydroxy or a group that with R^5 and with C/11 and C/12 carbon atoms forms a cyclic carbonate bridge;

provided that the linkage is through the nitrogen of Z at N/9a position or through the oxygen of R^3 at C/11 position.

6. The compound according to claim 2 wherein

Z is selested from >N-H, >N-CH_3, >N-C(O)NHR^x, wherein R^x is isopropyl;

W is >C=O or >CH_2 provided that when Z is >N-CH_3 W cannot be >C=O;

B is methyl;

E is hydrogen;

A is methyl;

R^2 is hydroxy or methoxy;

S^1 group represents a group of Formula **III** wherein

R^8 is selected from: amino, C_1-C_6-alkylamino, C_1-C_6-dialkylamino;

R^9 and R^{10} are hydrogen;

R^1 is O-S^2 wherein S^2 represents a group of Formula **IV** wherein R^{11} is hydrogen or O-R^{11} is a group that with R^{12} and with C/4"carbon atom forms a >C=O or epoxy group; R^{12} is hydrogen or a group that with O-R^{11} goup and with C/4"carbon atom forms a >C=O or epoxy group; R^{13} is methyl;

U is hydrogen;

Y is methyl;

R^3 is hydroxy;

R^4 is methyl;

R^5 is hydroxy or methoxy;

R^6 is ethyl;

provided that the linkage is through the nitrogen of R^8 at C/3', through the oxygen of R^2 at C/6 or through the carbon of R^{12} or through the oxygen of R^{11} both at C/4".

7. The compound according to claim 4 wherein

R^a and R^b independently represents, hydrogen or halogen;

R^d is hydrogen or hydroxy;

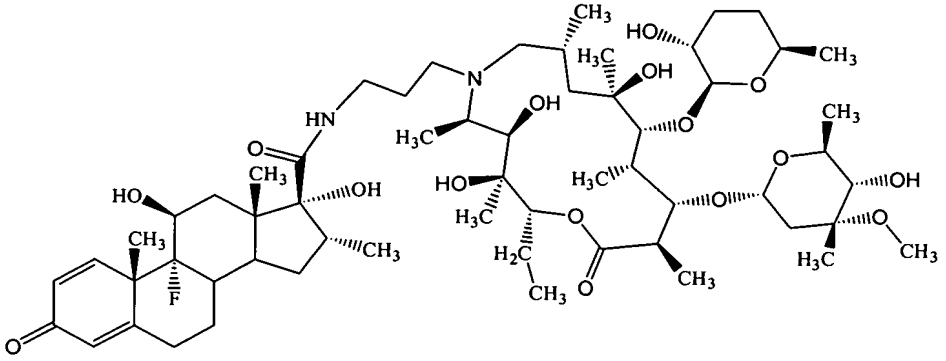
R^e is methyl;

R^f is hydroxy;

Rj is hydrogen

provided that the linkage is through the valence bond R^k.

8. A compound of the formula



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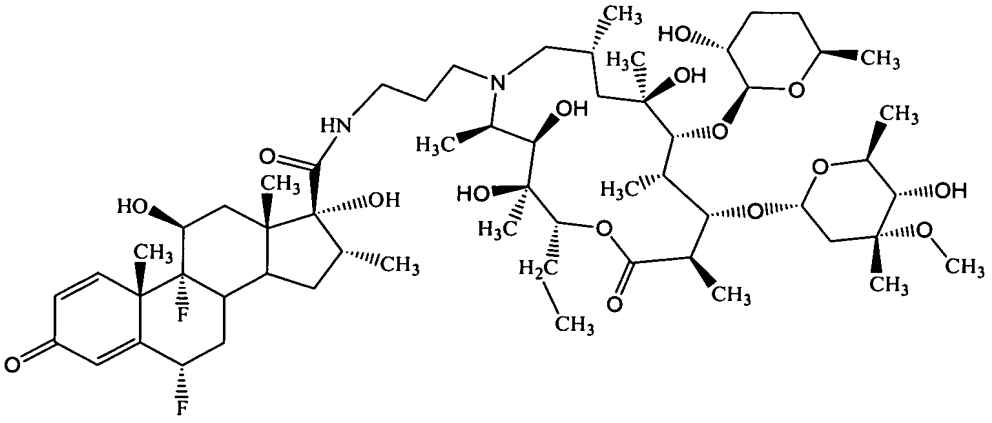

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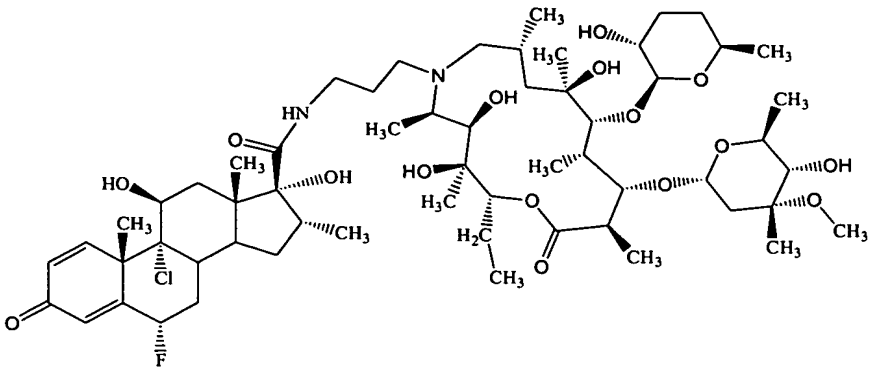

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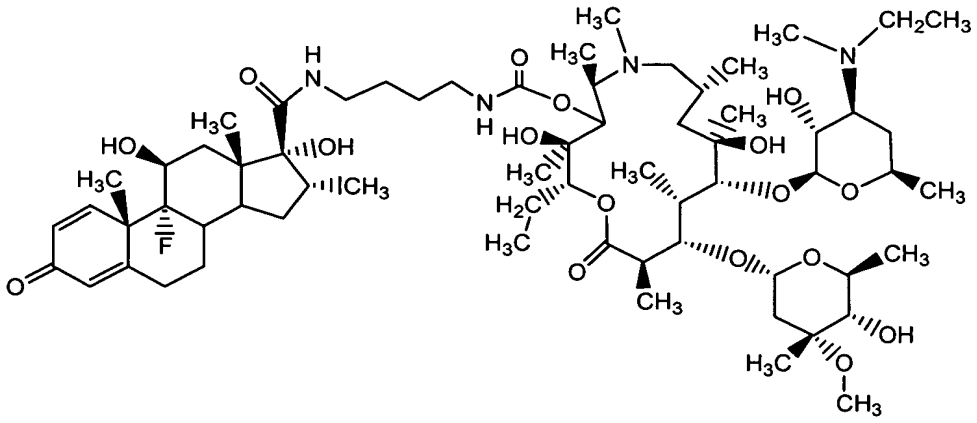

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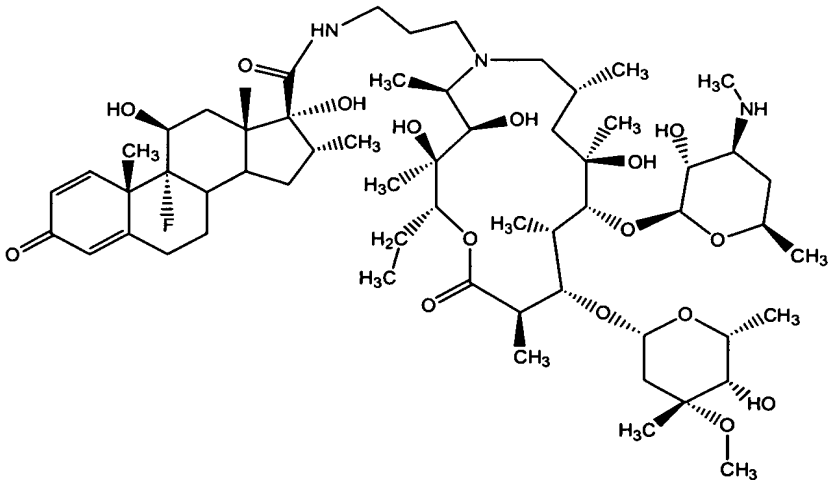

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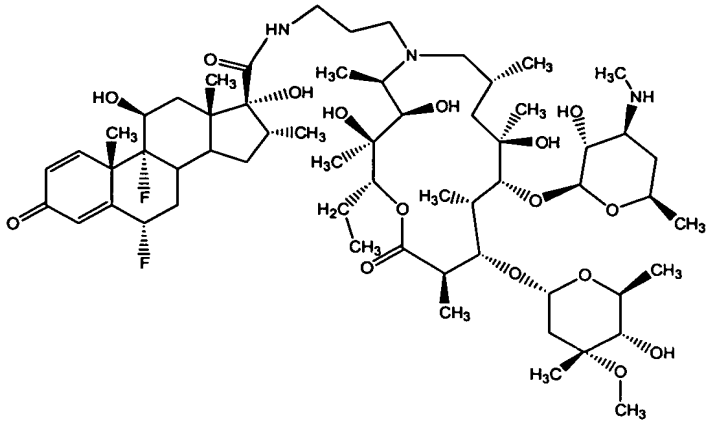

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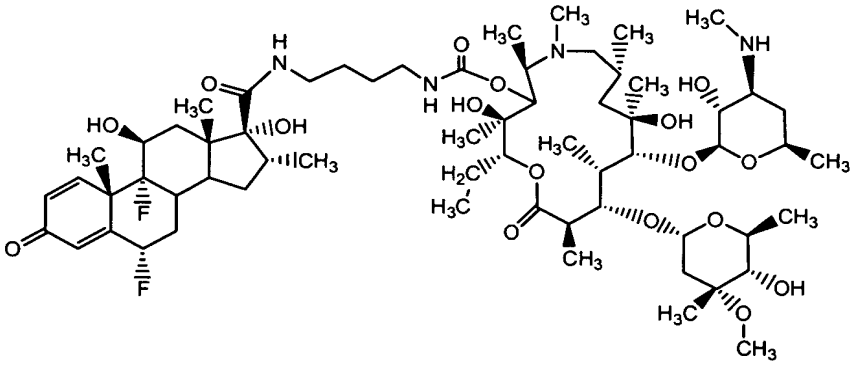

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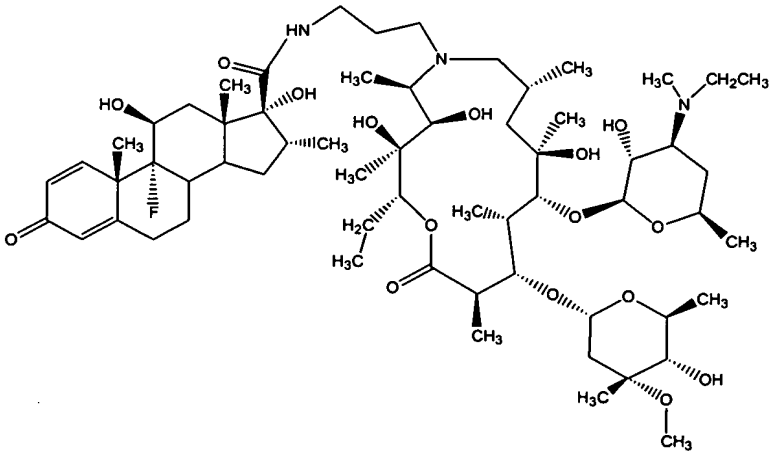

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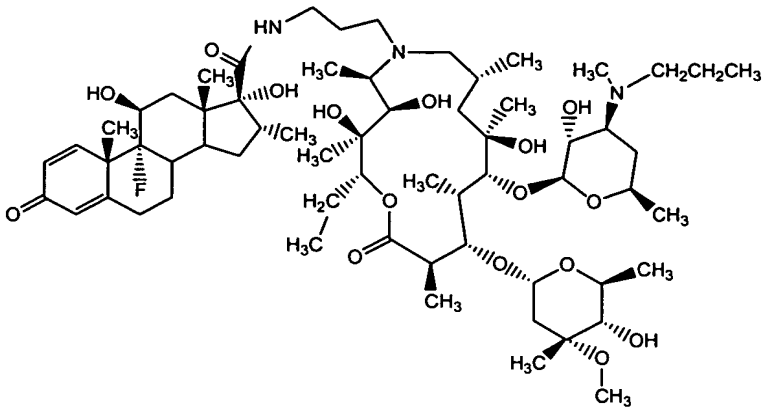

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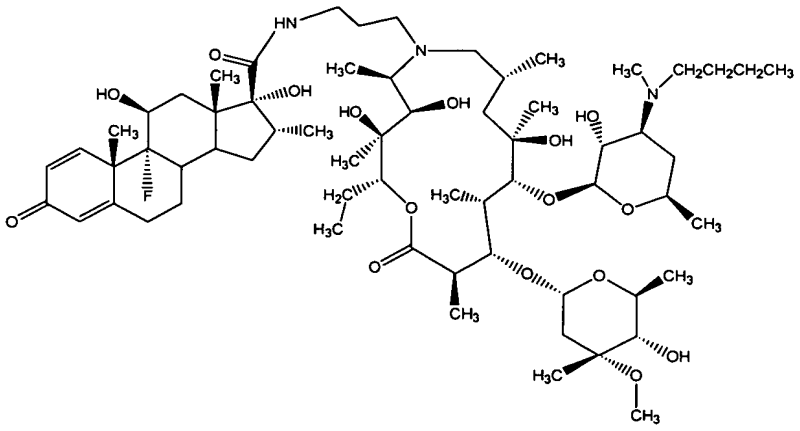

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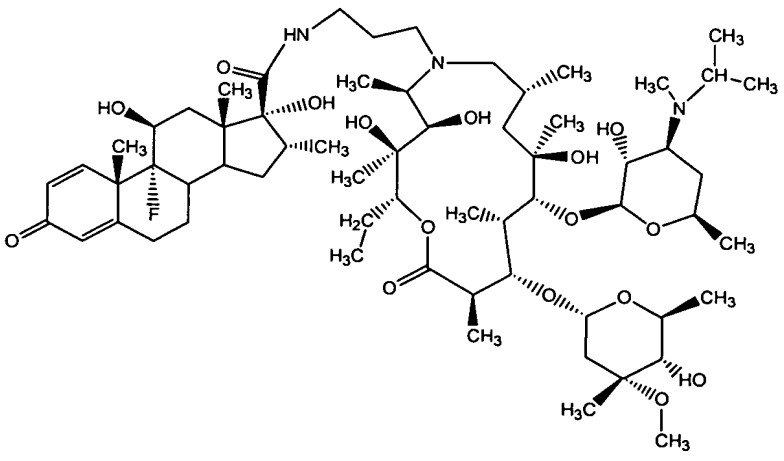

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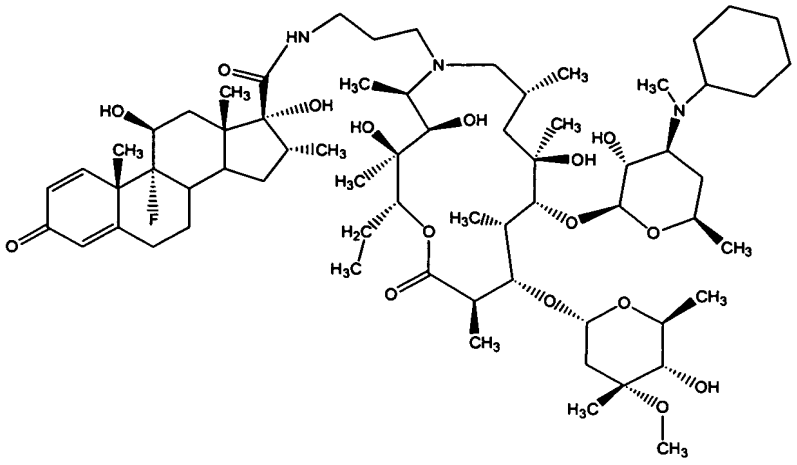

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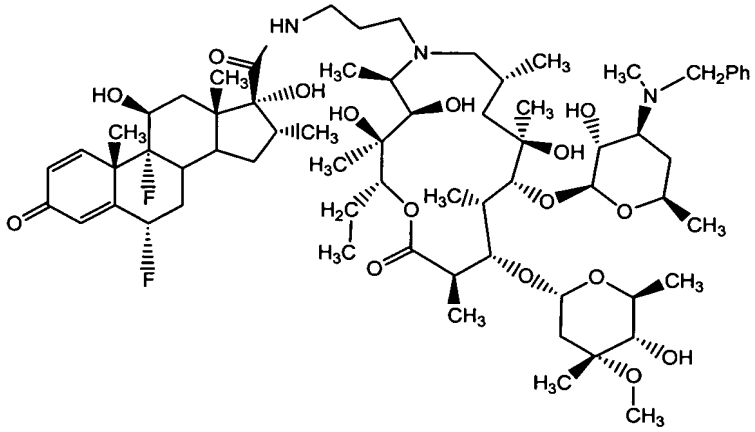

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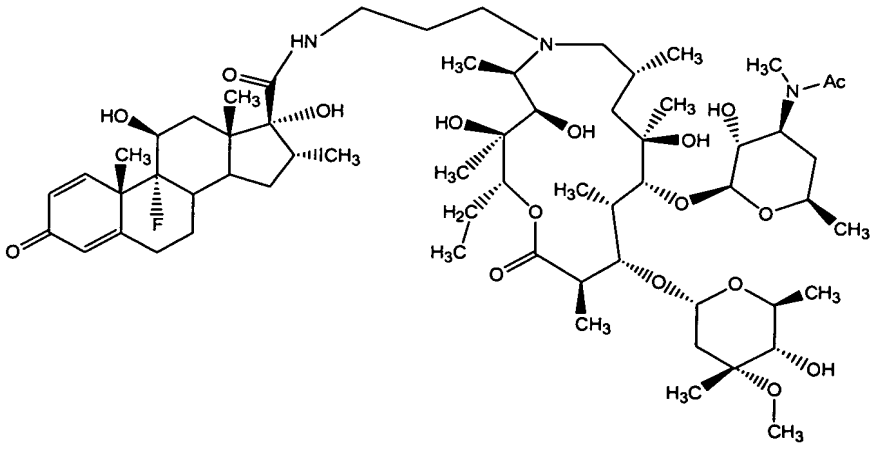

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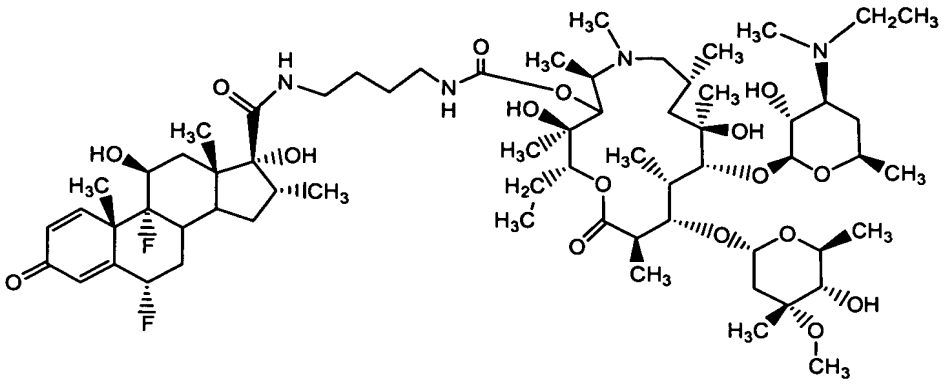

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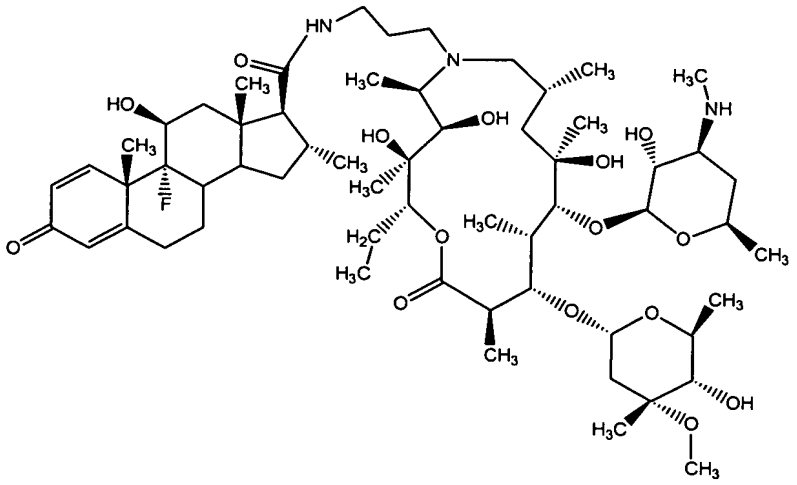

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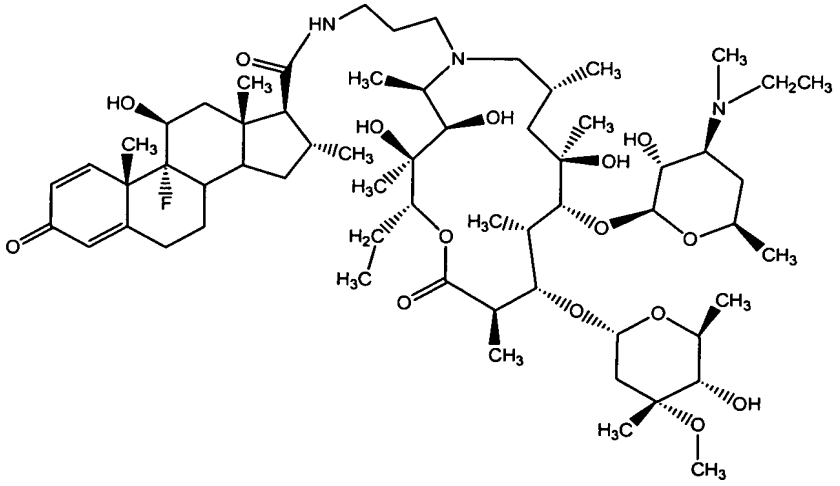

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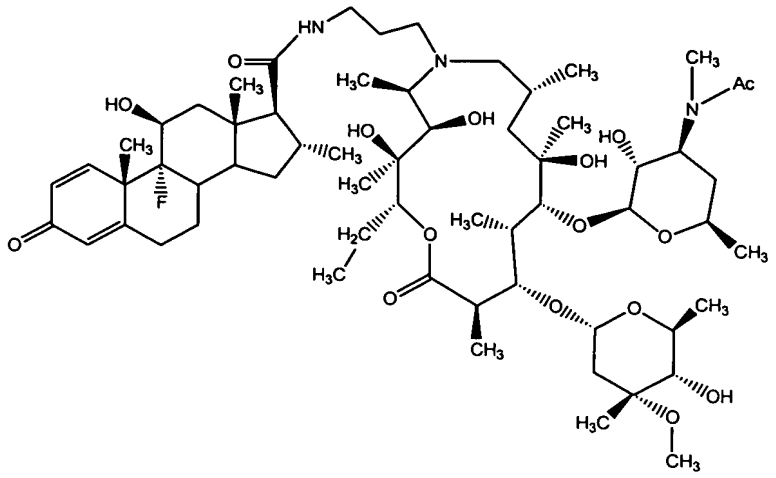

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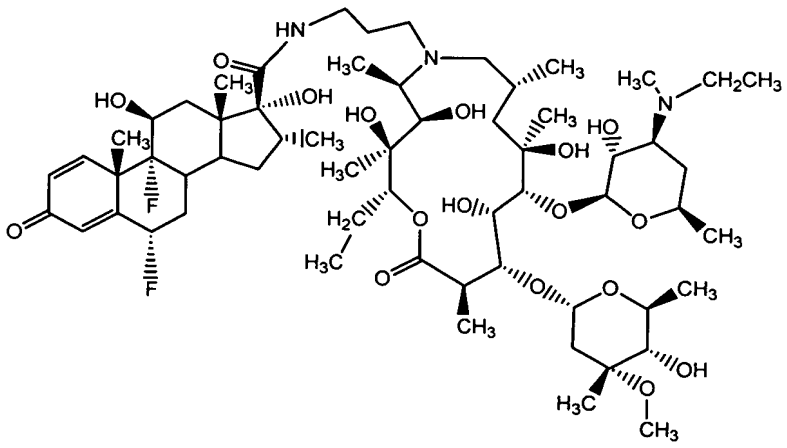

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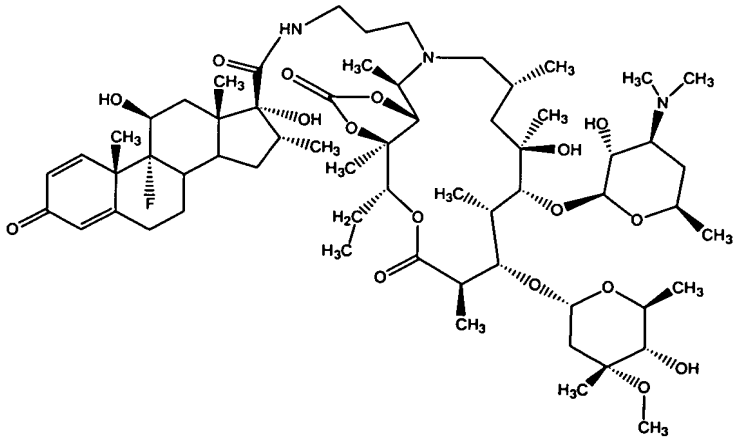

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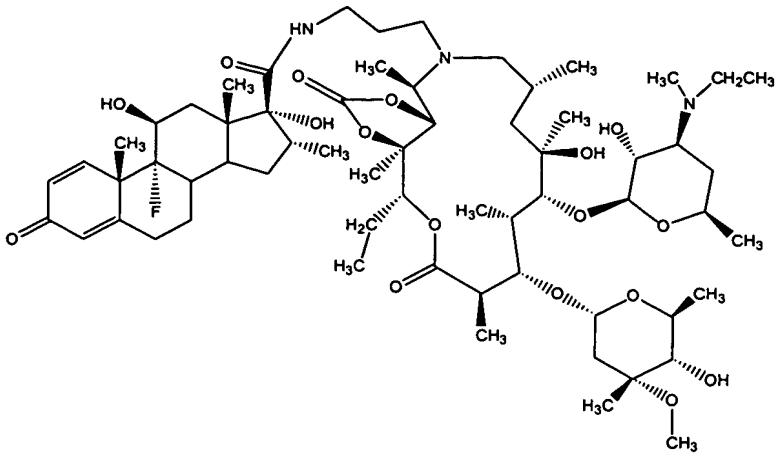

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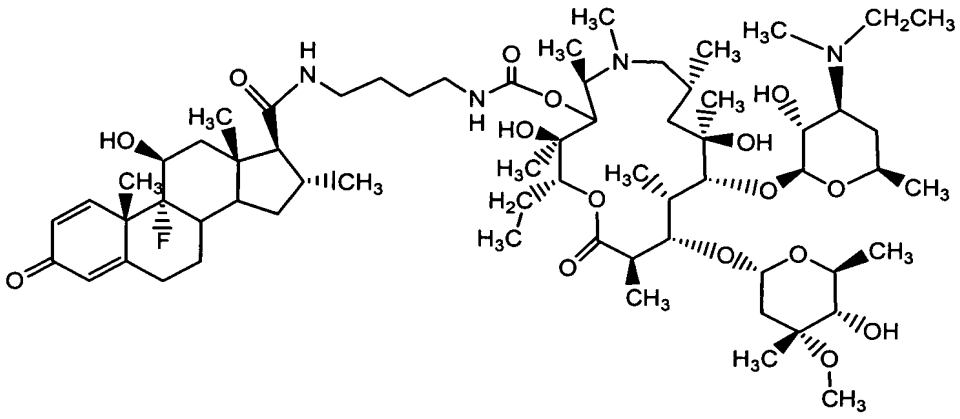

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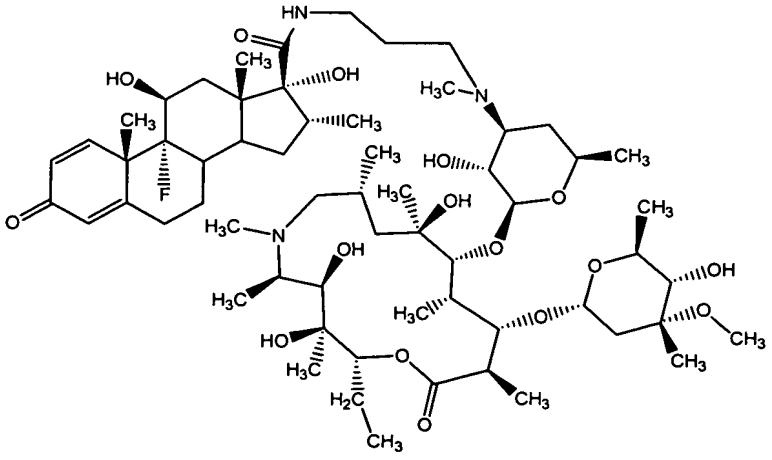

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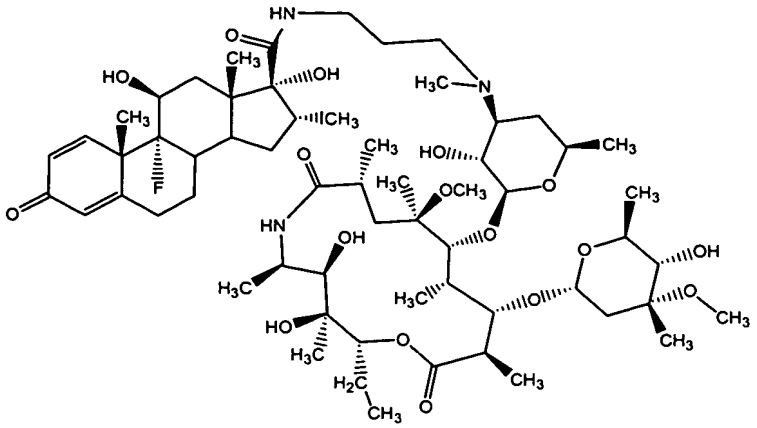

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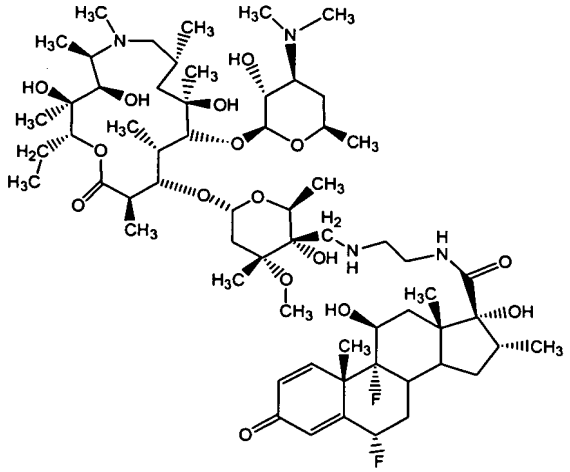

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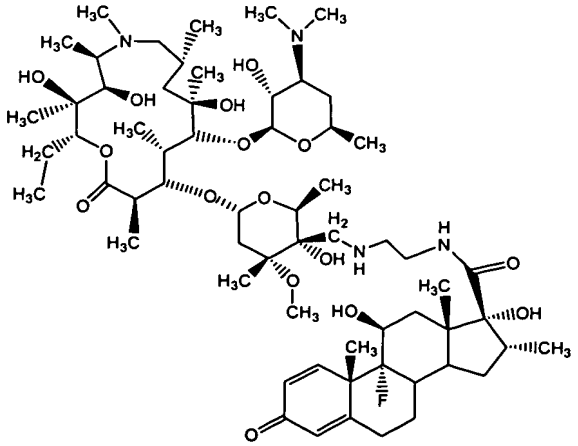

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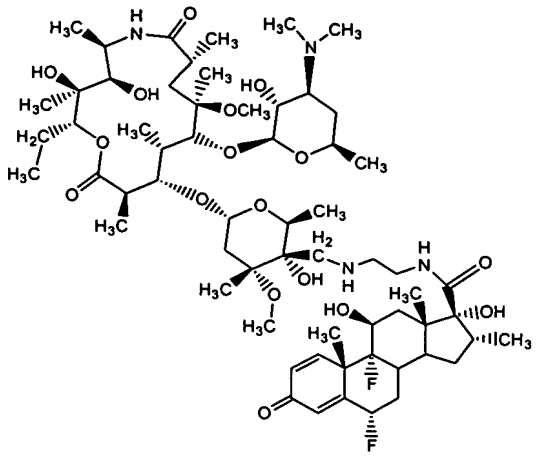

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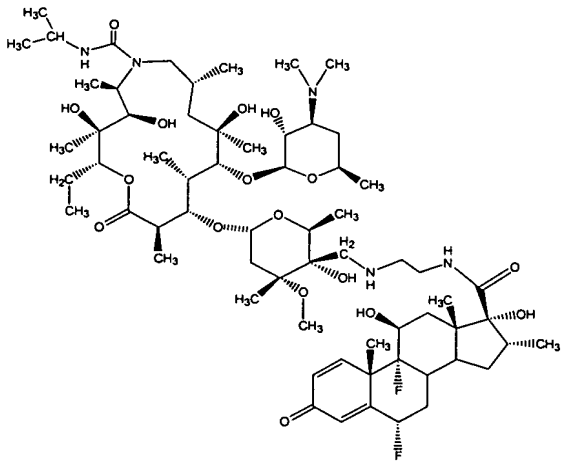

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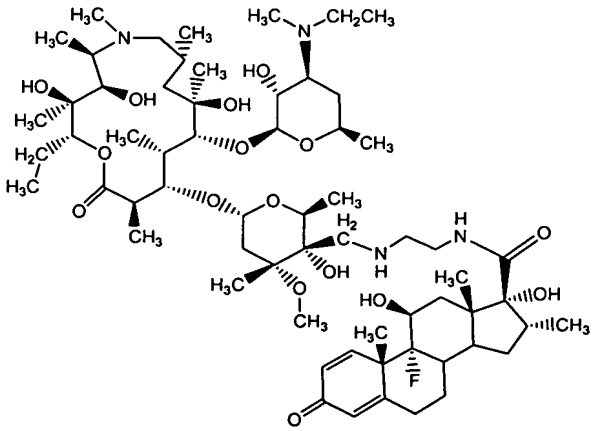

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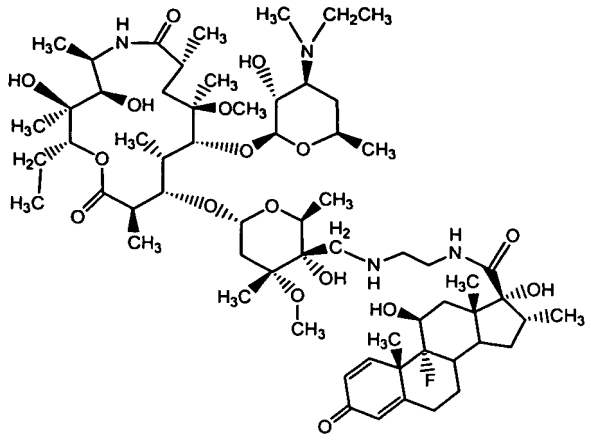

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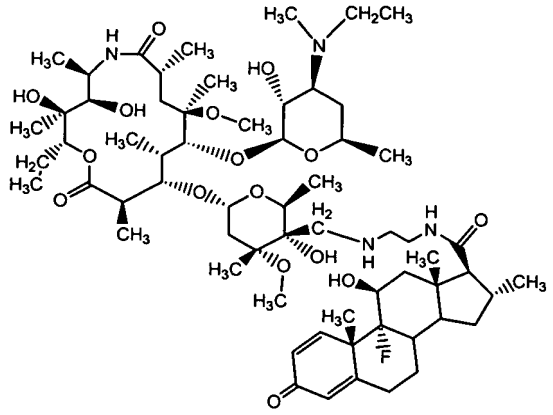

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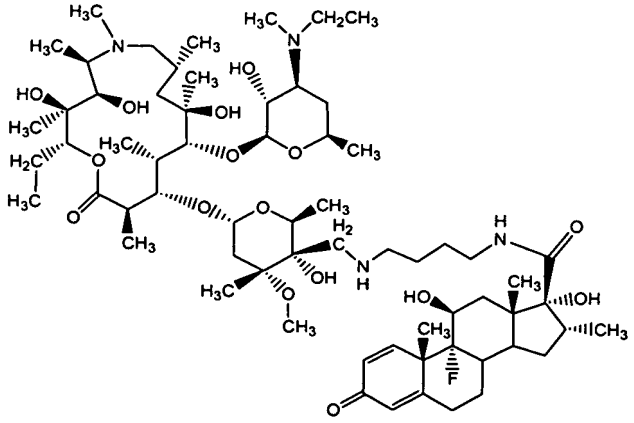

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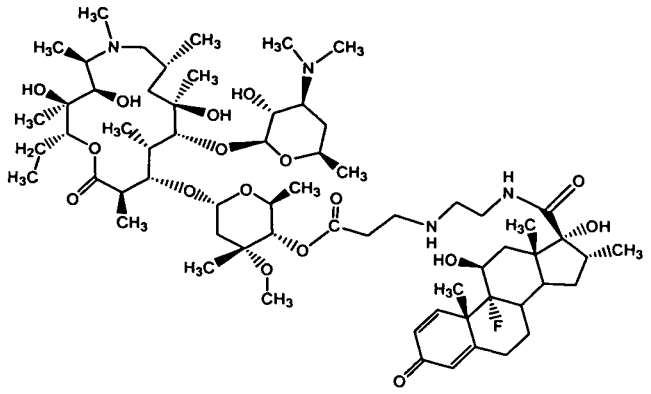

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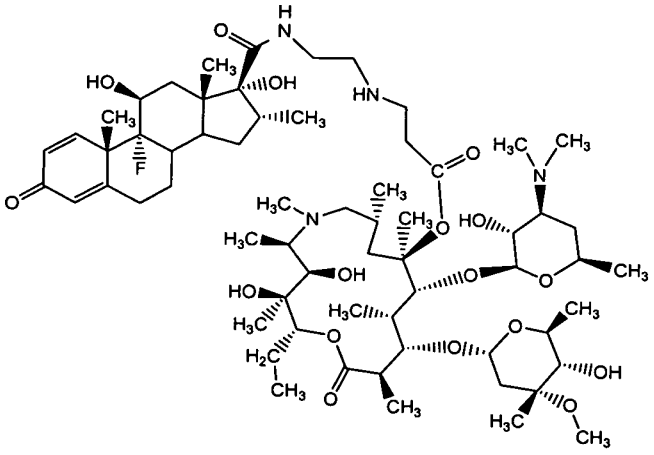

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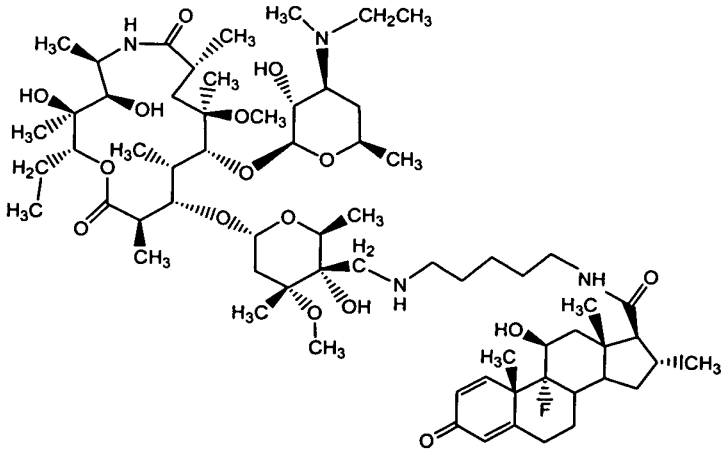
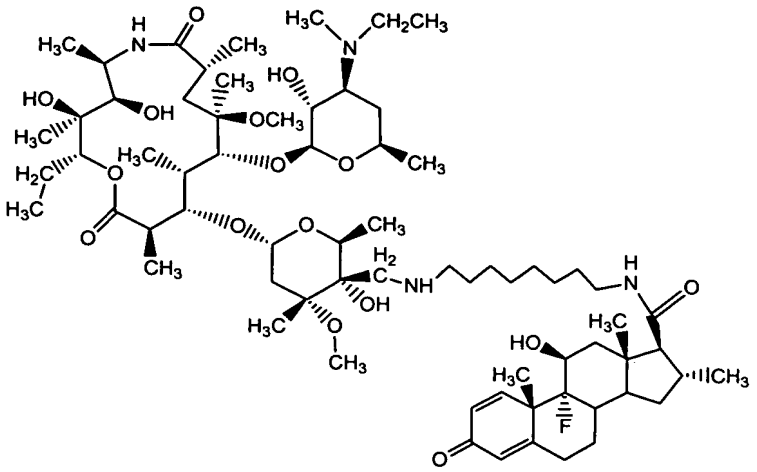
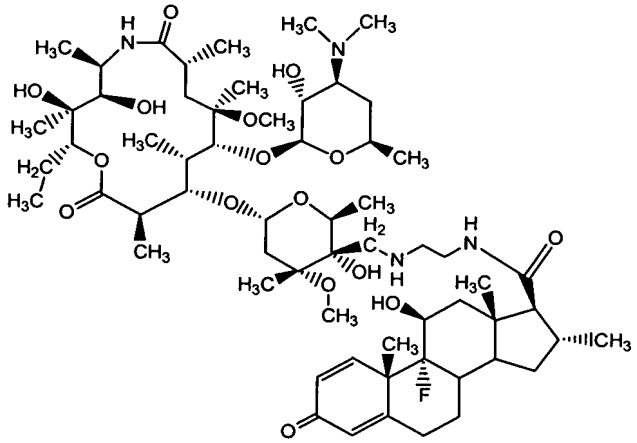


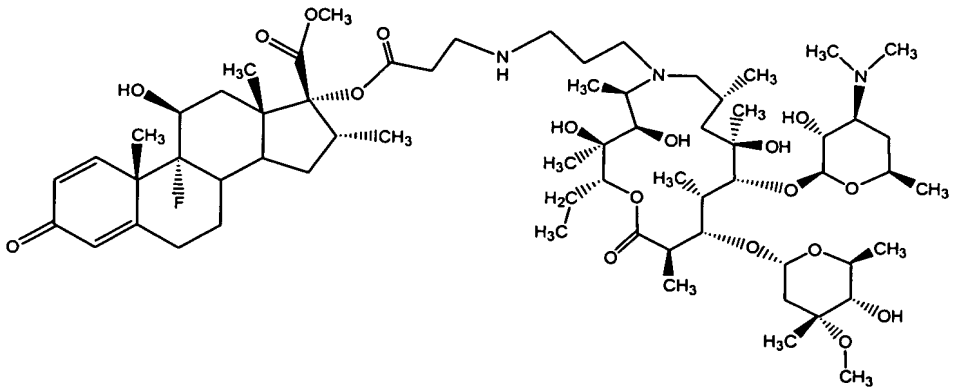
43. A compound of the formula



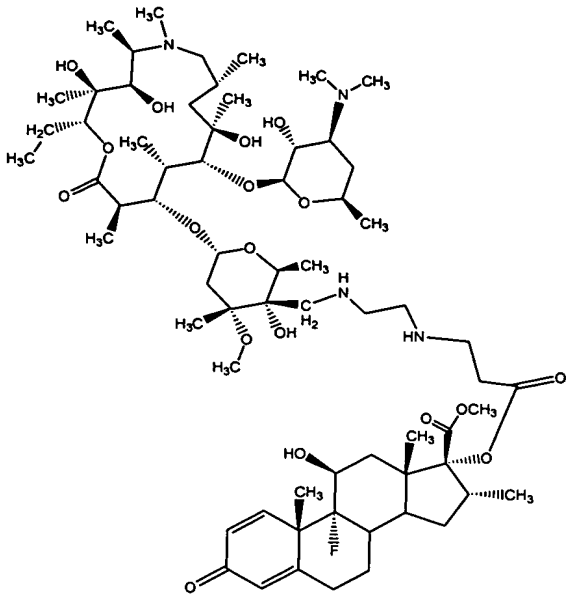
44. A compound of the formula



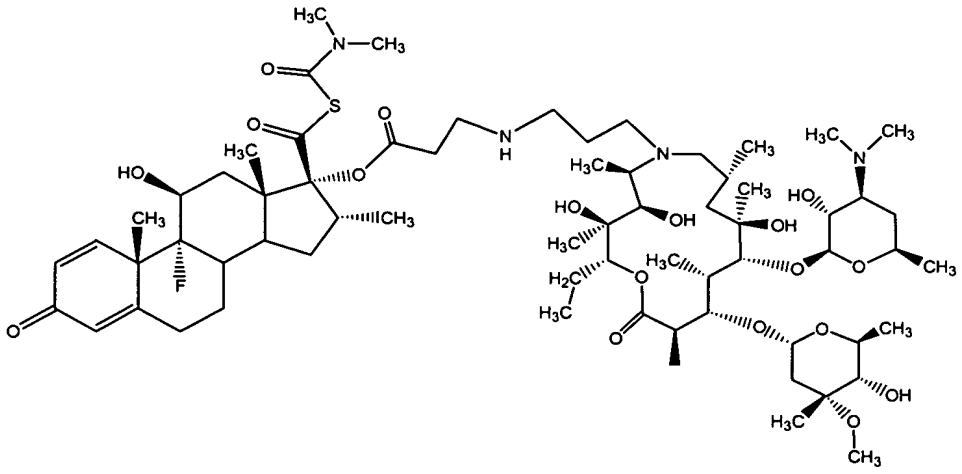
45. A compound of the formula



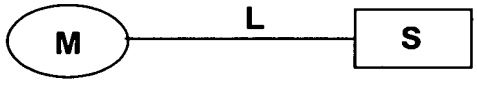
46. A compound of the formula



47. A compound of the formula

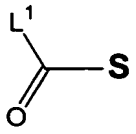


48. A process for the preparation for a compound of Formula **I** which comprises:



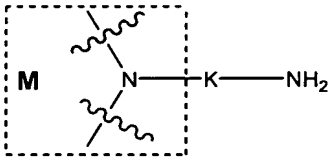
I

a) for a compound represented by Formula **I**, where X^2 is -NHC(O)-, by reacting a compound of Formula **V**:



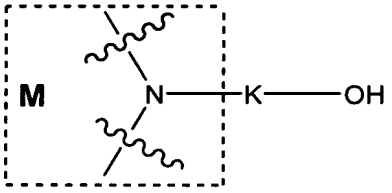
V

wherein L^1 represents a leaving group, and a free amino group of a macrolide represented by Formula **VId**:



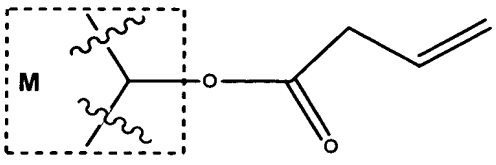
VId

b) for a compound represented by Formula **I**, where X^2 is -OC(O)-, by reacting a compound of Formula **V** and a hydroxyl group of a macrolide represented by Formula **VIe**:

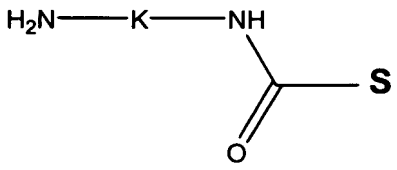


VIe

c) for a compound represented by Formula **I**, wherein X^1 is -OC(O)-, Q is NH and X^2 is -NHC(O)-, by reacting a macrolide represented by:

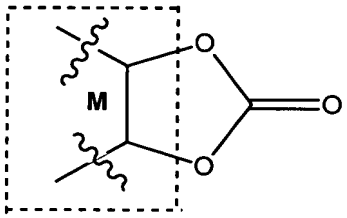


and a free amino group of the compound represented by Formula **IVc**:



IVc

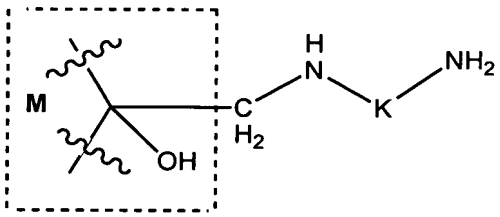
d) for a compound represented by Formula **I**, where X^1 is –OC(O)NH- and X^2 is -NHC(O)-, by reacting a macrolide represented by Formula **VII** and a free amino



group of Formula **IVc**:

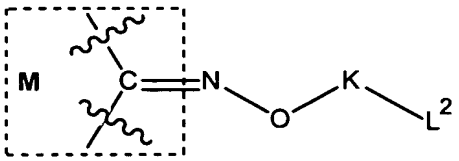
VII

e) for a compound represented by Formula **I**, where X^1 is $-CH_2-$, Q is -NH- and X^2 is -NHC(O)-, by reacting a macrolide represented by Formula **Va** and a compound of Formula **V**:

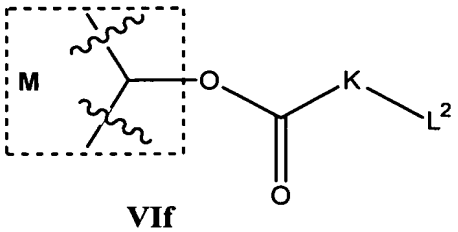


Va

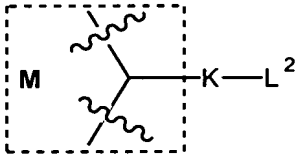
f) compound of Formula **I** by reacting a macrolide represented by Formula **VIf** or by Formula **VIg** or by Formula **VIh** having a leaving group L^2



VIh

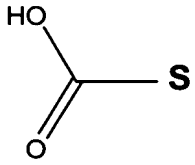


VIf



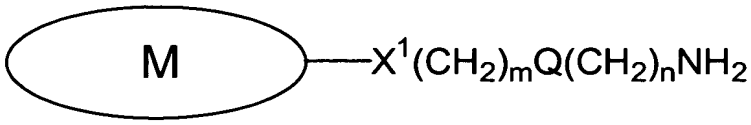
VIg

with a free carboxylic acid of steroid represented by Formula **IVb**.



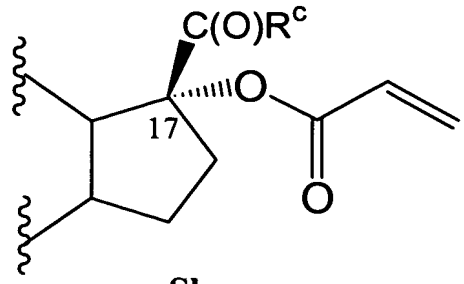
IVb

g) for a compound represented by Formula **I**, wherein X^1 is -OC(O)-, Q is NH and X^2 is -NH- by reacting a macrolide represented by:



VId

and a steroid subunit having a -C=C- bond represented by Formula **Sb**:



Sb

following by modification of R^c group;

49. A pharmaceutical composition comprising a compound according to claim 1 and pharmaceutically acceptable salts or solvate thereof as well as pharmaceutically acceptable diluent or carrier.

50. A method of treatment of inflammatory diseases, disorders and conditions characterized by or associated with an undesirable inflammatory immune response, and all diseases and conditions induced by or associated with an excessive secretion of TNF-α and IL-1 which comprises administering to a subject a therapeutically effective amount of a compound according to claim 1.

51. A method of treating inflammatory conditions and immune or anaphylactic disorders associated with infiltration of leukocytes into inflamed tissue in a subject in need thereof which comprises administering to said subject a therapeutically effective amount of the compound represented by Formula **I** or a pharmaceutically acceptable salts or solvate thereof.

52. The method according to claim 51, wherein inflammatory conditions and immune disorders are selected from the group consisting of asthma, adult respiratory distress syndrome, bronchitis, and cystic fibrosis.

53. A method according to claim 51, wherein said inflammatory conditions and immune disorders are selected from the group consisting of inflammatory conditions or immune disorders of the lungs, joints, eyes, bowel, skin, and heart.

54. A method according to claim 51, wherein said inflammatory conditions and immune disorders are selected from the group consisting of asthma, adult respiratory distress syndrome, bronchitis, cystic fibrosis, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, uveitis, conjunctivitis, inflammatory bowel conditions, Crohn's disease, ulcerative colitis, distal proctitis, psoriasis, eczema, dermatitis, coronary infarct damage, chronic inflammation, endotoxin shock, and smooth muscle proliferation disorders.